Heuristic Reevaluation of the Bacterial Hypothesis of Peptic Ulcer Disease in the 1950s

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Many historical accounts of the research on peptic ulcer disease (in short, PUD) roughly distinguish three phases separated by two landmark studies. In the first phase (from the second half of the 19th century to 1954) two main hypotheses were investigated in parallel: on the one hand, the acidity hypothesis according to which the cause of PUD was gastric acid, and on the other hand, the bacterial hypothesis according to which the cause of PUD were bacteria. Neither hypothesis gained a decisive break-through in terms of theory confirmation, nor suffered from severe refutations. The situation changed in 1954 with the publication of a large-scale study by Palmer (1954) which challenged the bacterial hypothesis with serious refutatory counter-evidence. According to (Kidd & Modlin, 1998, p. 10), Palmer's study "may be credited with the envious distinction of setting back gastric bacterial research by a further 30 years". Similarly, Fukuda et al. (2002) suggest that Palmer's study "established the dogma that bacteria could not live in the human stomach, and as a result, investigation of gastric bacteria attracted little attention for the next 20 years" (p. 20). Only in the 1980s the bacterial hypothesis had its come-back, culminating in a study by Warren and Marshall (1983; 1984), who managed to identify one of the main causes of PUD in Helyobacter Pylori. After their results have been confirmed by other scientists, the bacterial hypothesis was accepted (Thagard (2000), Solomon (2001)), and in 2005 Warren and Marshall were awarded the Nobel Prize in Physiology or Medicine for this discovery.

In this paper we investigate the status of the bacterial hypothesis after the publication of Palmer's study. We focus on the question whether the bacterial hypothesis was still worthy of further pursuit at this time. According to some scholars, Palmer's study had an impact of a crucial experiment, which clearly refuted the bacterial hypothesis. For instance, (Zollman, 2010, p. 21) writes that after Palmer's results "everything was 'done by the book' " and that "one can hardly criticize their [the researcher's] behavior" when abandoning the bacterial hypothesis until the new study of Warren and Marshall turned the tables. Hence should Zollman's assessment be adequate, our question regarding the pursuit worthiness of the bacterial hypothesis would have to be answered with a decisive "no".

We argue for the following two theses:

The perceived refutatory impact of Palmer's study is disproportionate to its methodological rigor. This undermines its perceived status as a crucial experiment against the bacterial hypothesis. Of special interest for our research question is the staining method used for detecting bacteria in Palmer's study. We begin our inquiry by asking what Warren and Marshal did differently 30 years later that allowed them to demonstrate the bacteria. The key difference in their method is the type of staining which the latter authors applied to the specimens under examination. In contrast to Palmer who used hematoxylin and eosin (H&E) impregnation, which is an excellent stain for displaying tissue morphology, Warren and Marshall applied silver staining, which showed Helicobacter well enough (Marshall & Warren, 1984). The question which immediately comes up is why Palmer did not use silver staining, or more precisely: Was the method of silver staining already well known by 1954 (the year when Palmer's article was published)?

In case the method of silver staining was indeed well known by this time, were there good epistemic reasons available already at that time, that silver staining should have been considered a significant

method for the detection of spirochetes in gastric mucosa?

Were the shortcomings of the H&E method known by 1954, especially in the context in which it was used in Palmer's study? In other words, were there good reasons available at the time, that the H&E method should have been considered possibly problematic for the detection of certain spirochetes in gastric mucosa?

By answering these questions we are able to evaluate the reliability of Palmer's results.

In view of this and other considerations we argue that the bacterial hy- pothesis was worthy of pursuit in the 1950s. The question of the pursuit worthiness is best answered by means of a heuristic appraisal. Two concerns are of importance to this end:

The question whether there was enough of a protective belt for the bacterial hypothesis to give researchers – in Lakatos' wording – a "rational scope for dogmatic adherence to [their] programme in face of prima facie 'refutations' " (Lakatos, 1978, p. XX) such as Palmer's study. This concerns the question of negative heuristics.

The question whether the bacterial hypothesis was not stuck in terms of available research options. This concerns the question of positive heuristics which opens research venues and hence gives researchers problems or puzzles to work on and, in turn, options to refine and improve on their previous models. The philosophical message to take home from this case is a message of the potential fruitfulness of methodological critical scrutiny for the practicing re- searchers on the one hand, and the fruitfulness of a close reading of the historical material for the philosopher interested in case studies on the other hand. Moreover, Zollman (2010) uses this case study to illustrate why scientific progress would benefit from a restricted information flow among scientists. Our results suggested the opposite: that the information flow among scientists was subop- timal in this particular case. We close the paper by mentioning a number of sociological and other factors that require further examination for this thesis to be substantiated.

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